Antibiotico-resistenza: fenomeno anche di genere?

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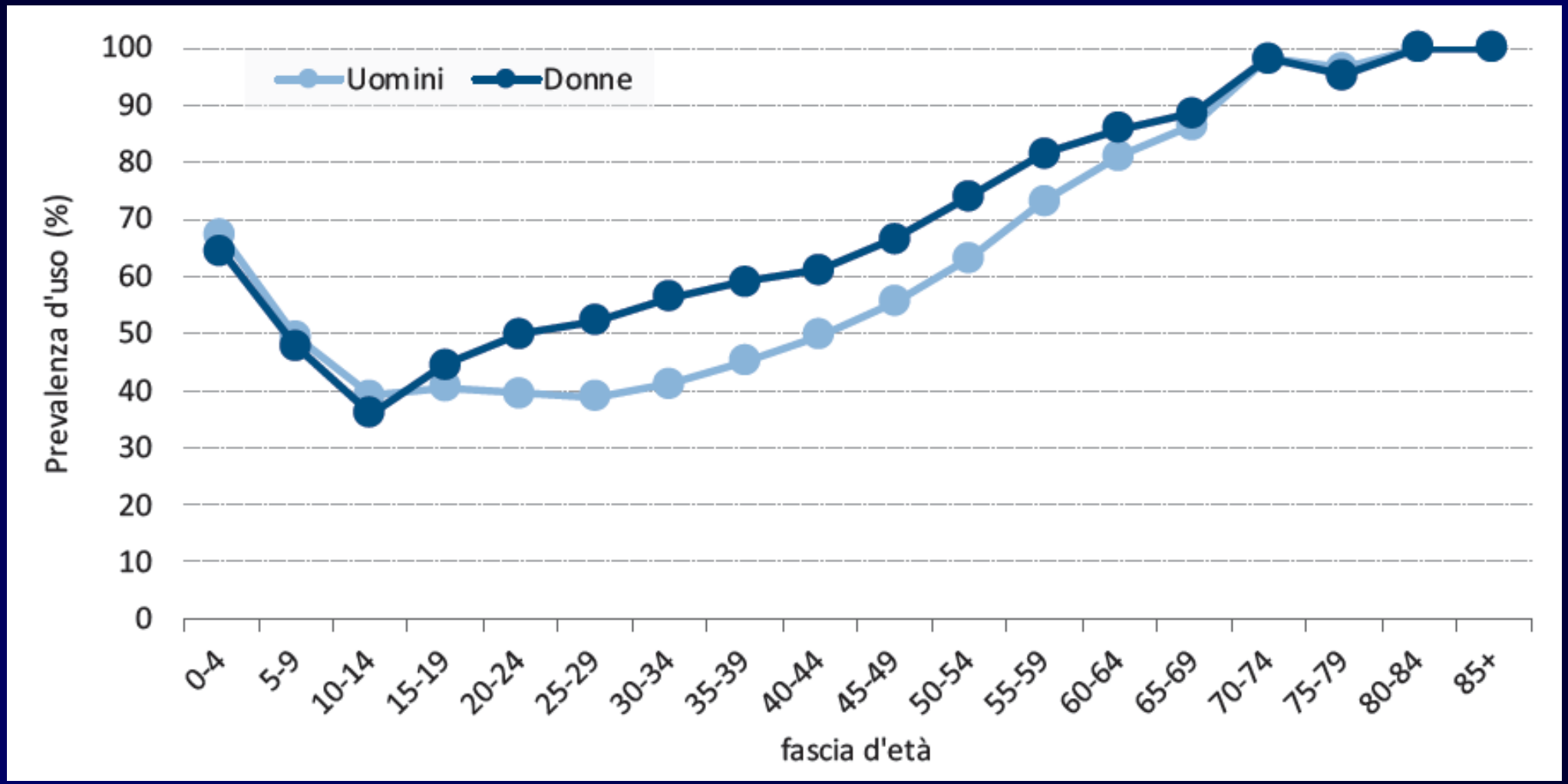
UNIVERSITÀ DEGLI STUDI FIRENZE

- **Le donne sono le maggiori consumatrici di molte classi di farmaci** (es. antidolorifici, antidepressivi, antibiotici, eccetto farmaci cardio vascolari)
- **Le donne rispondono in maniera diversa rispetto all'uomo ai farmaci** (differenze fisiologiche, anatomiche e ormonali)
- **Le donne mostrano un profilo farmacocinetico peculiare** per assorbimento, distribuzione, metabolismo ed eliminazione dei farmaci
- Hanno un peso corporeo medio inferiore all'uomo, una percentuale di massa grassa più alta, un minore volume plasmatico ed un profilo di legame tra farmaco e proteine plasmatiche diverso

Franconi F, Campesi I, Expert Rev Clin Pharmacol 2014; Mazzei T et al, Gender-Related Health in Tuscany, Regional Health Agency of Tuscany, June 2015

Andamento della prevalenza d'uso per età e genere dei farmaci territoriali nel 2018

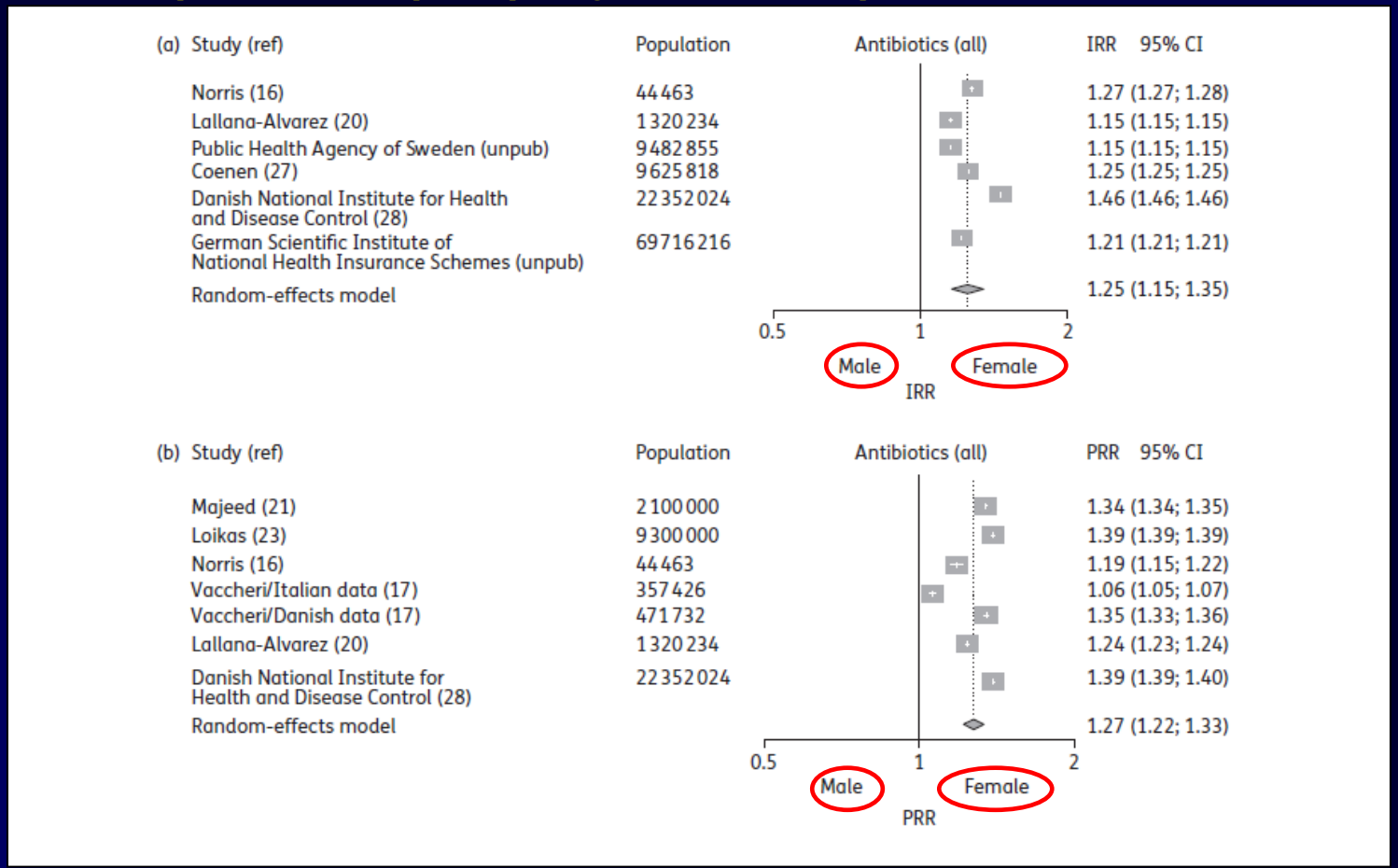


L'uso dei Farmaci in Italia – Rapporto nazionale Anno 2018, AIFA 18/07/2019

Differenze di genere nella prescrizione di antibiotici in comunità: revisione sistematica della letteratura e meta-analisi

Wiebke Schröder[1,2], Harriet Sommer[3,4], Beryl Primrose Gladstone[1], Federico Foschi[1,2], Jenny Hellman[5], Birgitta Evengard[6] and Evelina Tacconelli[1,2]*

(a) Meta-analisi delle prescrizioni di antibiotici in comunità misurata come rapporto tra i tassi di incidenza (IRR) di DDD prescritte/1000 abitanti/die; (b) rapporto tra i tassi di prevalenza (PRR) degli antibiotici prescritti/1000 abitanti



J Antimicrob Chemother, Advance Access published Apri 3, 2016

DDD, dose media di un farmaco assunta giornalmente da un paziente adulto, con riferimento all'indicazione terapeutica principale del farmaco stesso

Indications and classes of outpatient antibiotic prescriptions in Japan: A descriptive study using the national database of electronic health insurance claims, 2012–2015

Annual antibiotic prescription by antibiotic category and sex by age (2012–2015)

Characteristics	Annual antibiotic prescription [a]	
	All ages	
	N[b]	Rate[c]
Overall	89.6	704
Sex		
Male	40.2	650
Female	49.3	755
Antibiotic category		
3rd cephem	33.1	260
Macrolides	25.8	203
Quinolones	18.2	143

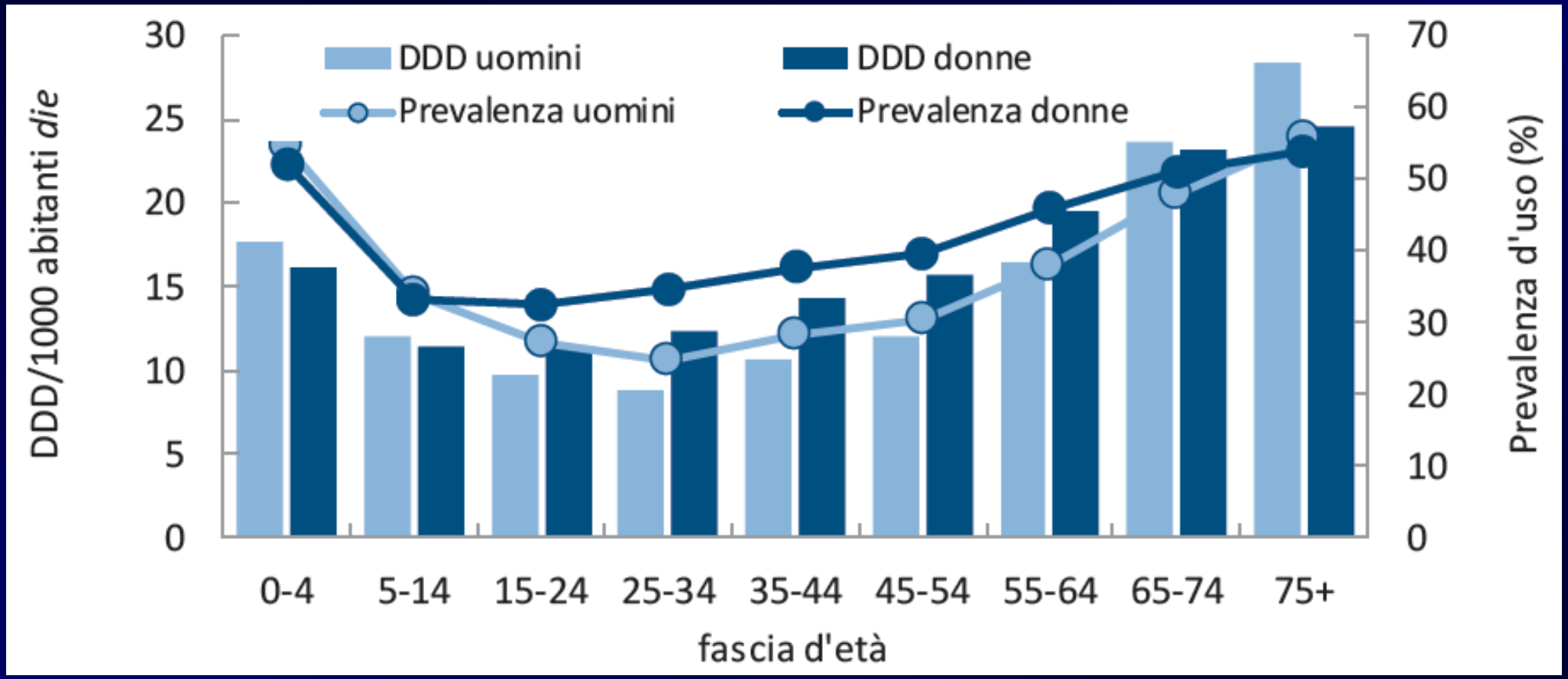
a) Different antibiotics were counted separately if multiple antibiotics were prescribed on the same day.

b) Number of visits with antibiotic prescriptions per year (in millions).

c) Rate of visits with antibiotic prescriptions per 1000 population per year.

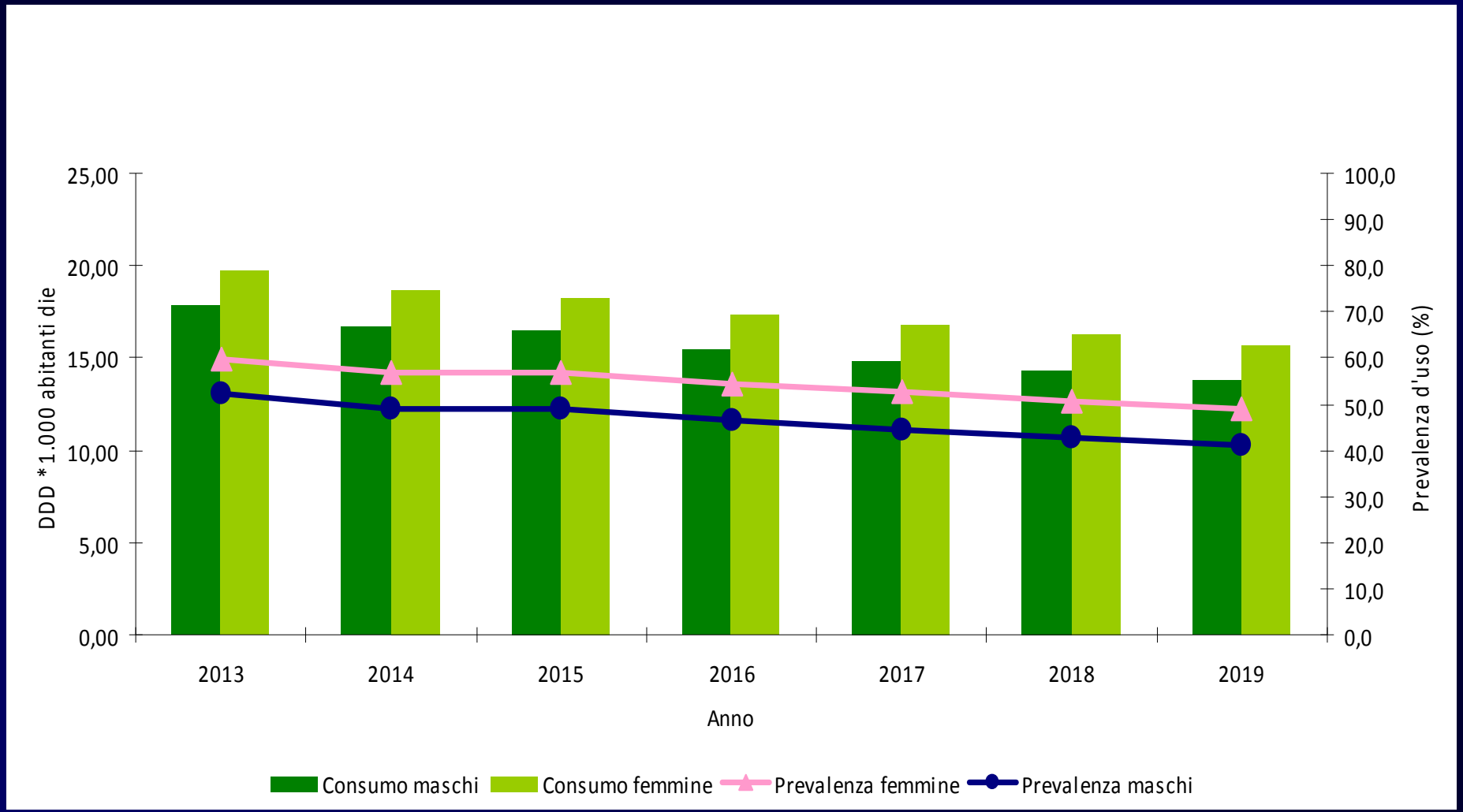
Hashimoto et al., Int J Infect Dis, 2020

Distribuzione della prevalenza d'uso e del consumo 2018 di antibiotici in regime di assistenza convenzionata

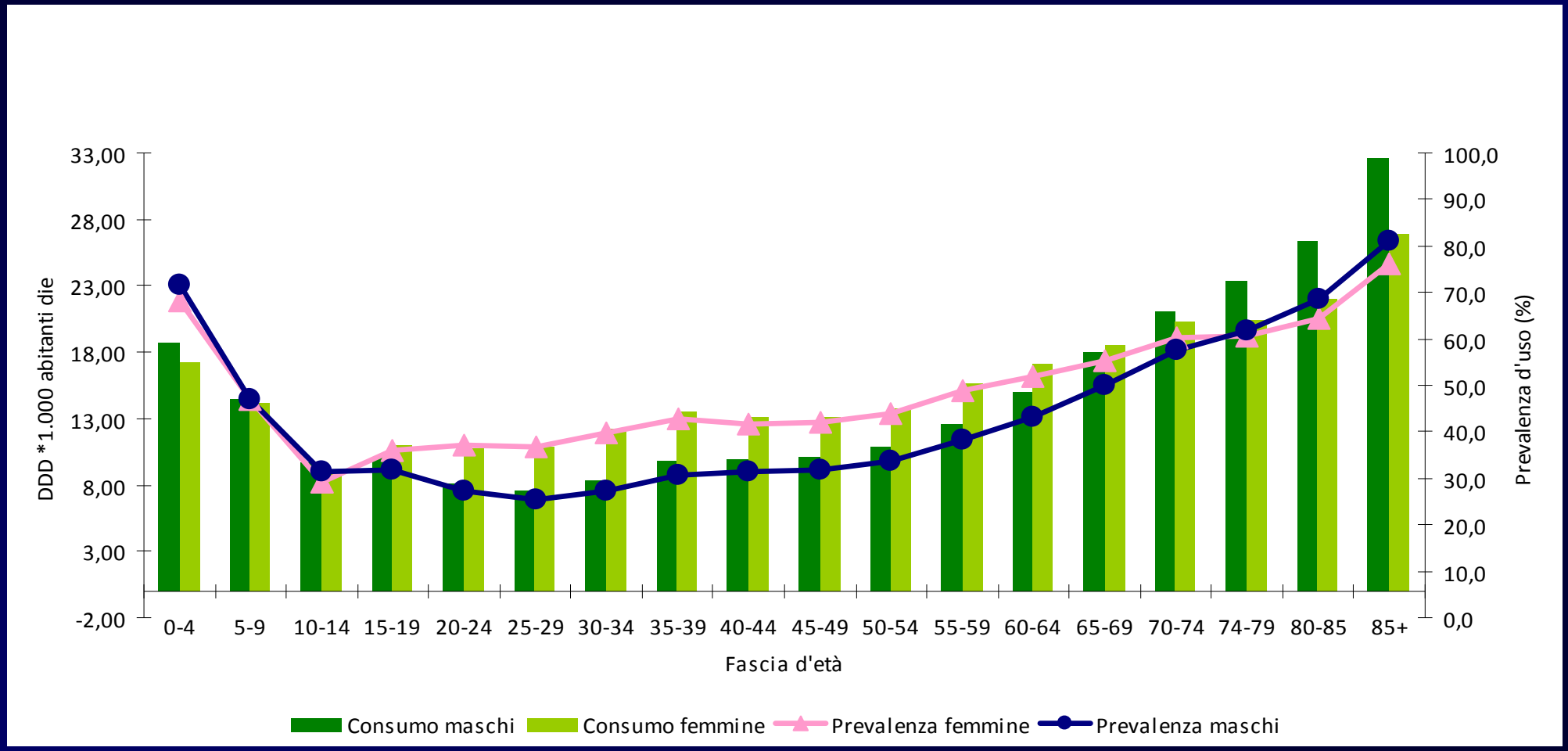


L'uso dei Farmaci in Italia – Rapporto nazionale Anno 2018, AIFA 18/07/2019

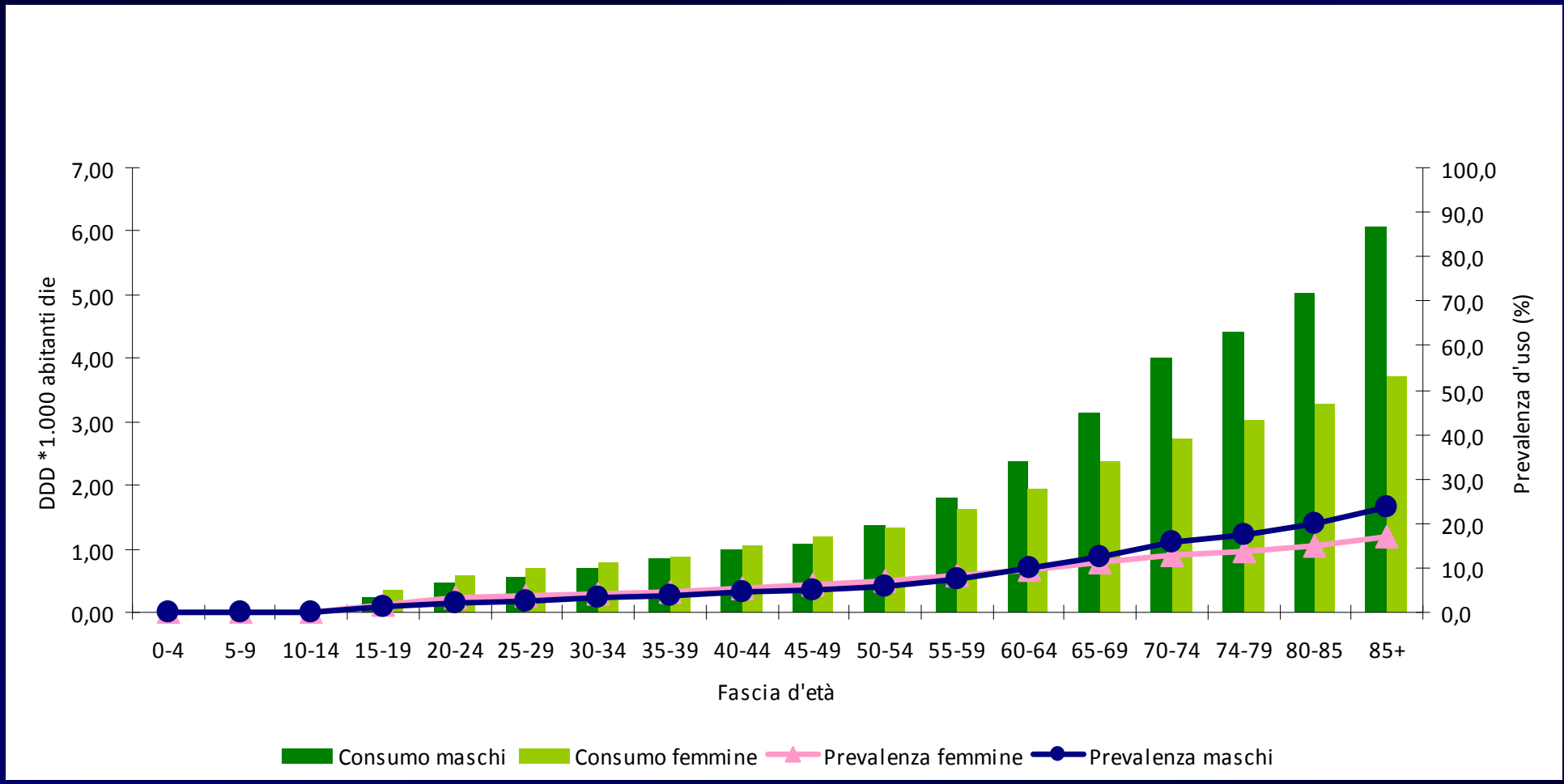
Consumo e prevalenza d'uso di antimicrobici ad uso sistemico (ATC J01) per anno e sesso Toscana 2013-2019 (ARS)



Consumo e prevalenza d'uso di antimicrobici ad uso sistemico (ATC J01) per sesso e classe di età Toscana 2013-2019 (ARS)

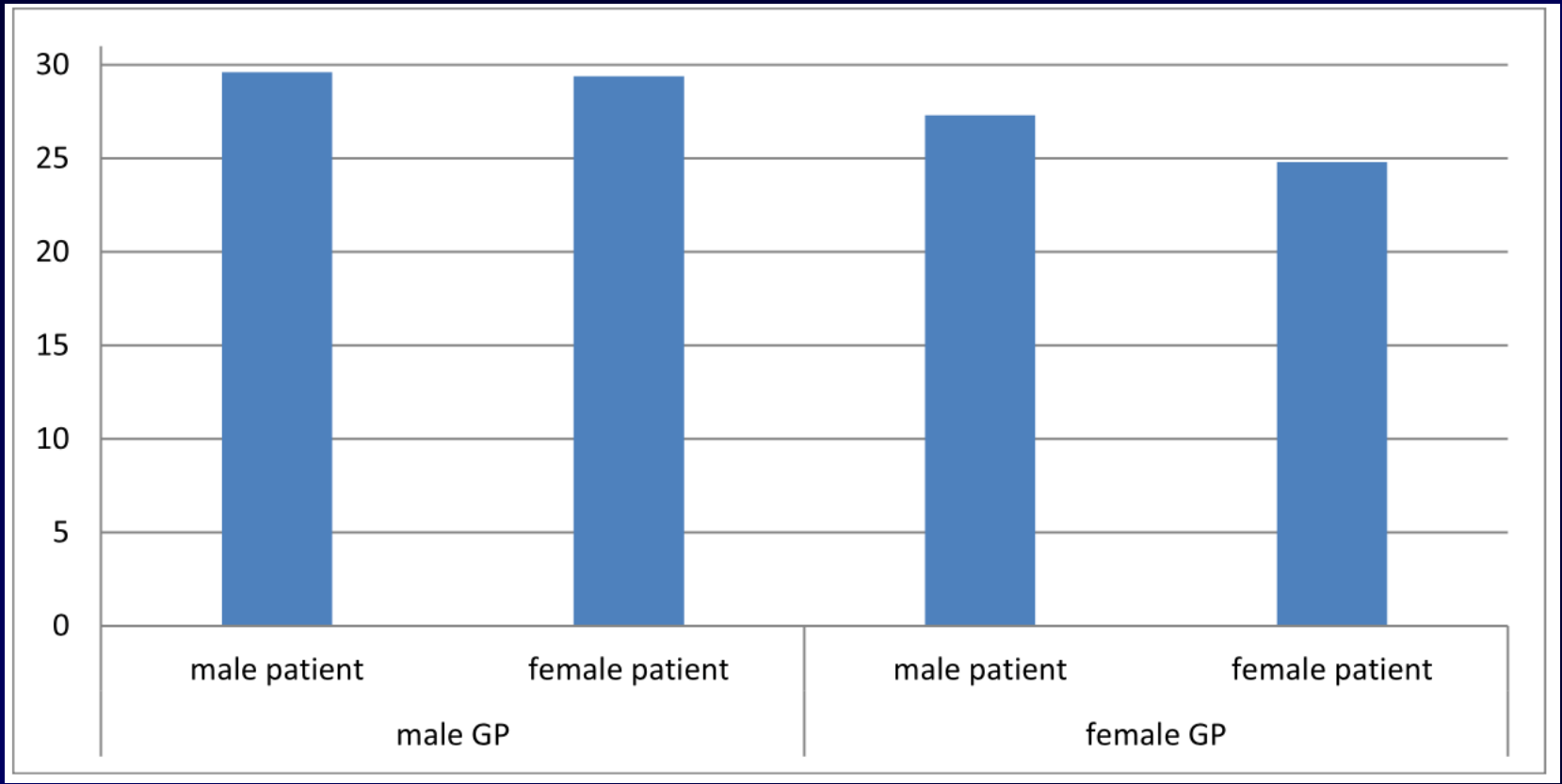


Consumo e prevalenza d'uso di fluorochinoloni (ATC J01MA) per sesso e classe di età Toscana 2019 (ARS)



The influence of gender concordance between general practitioner and patient on antibiotic prescribing for sore throat symptoms: a retrospective study

Percentage of 11,285 GP consultations for sore throat symptoms with antibiotic prescription (The Netherlands 2013)



Female GP's prescribe antibiotics less often than male GP's (p = .000). In dyads with a female GP, antibiotics are less often prescribed when there is gender concordance (p = .044); GP, General Practitioner

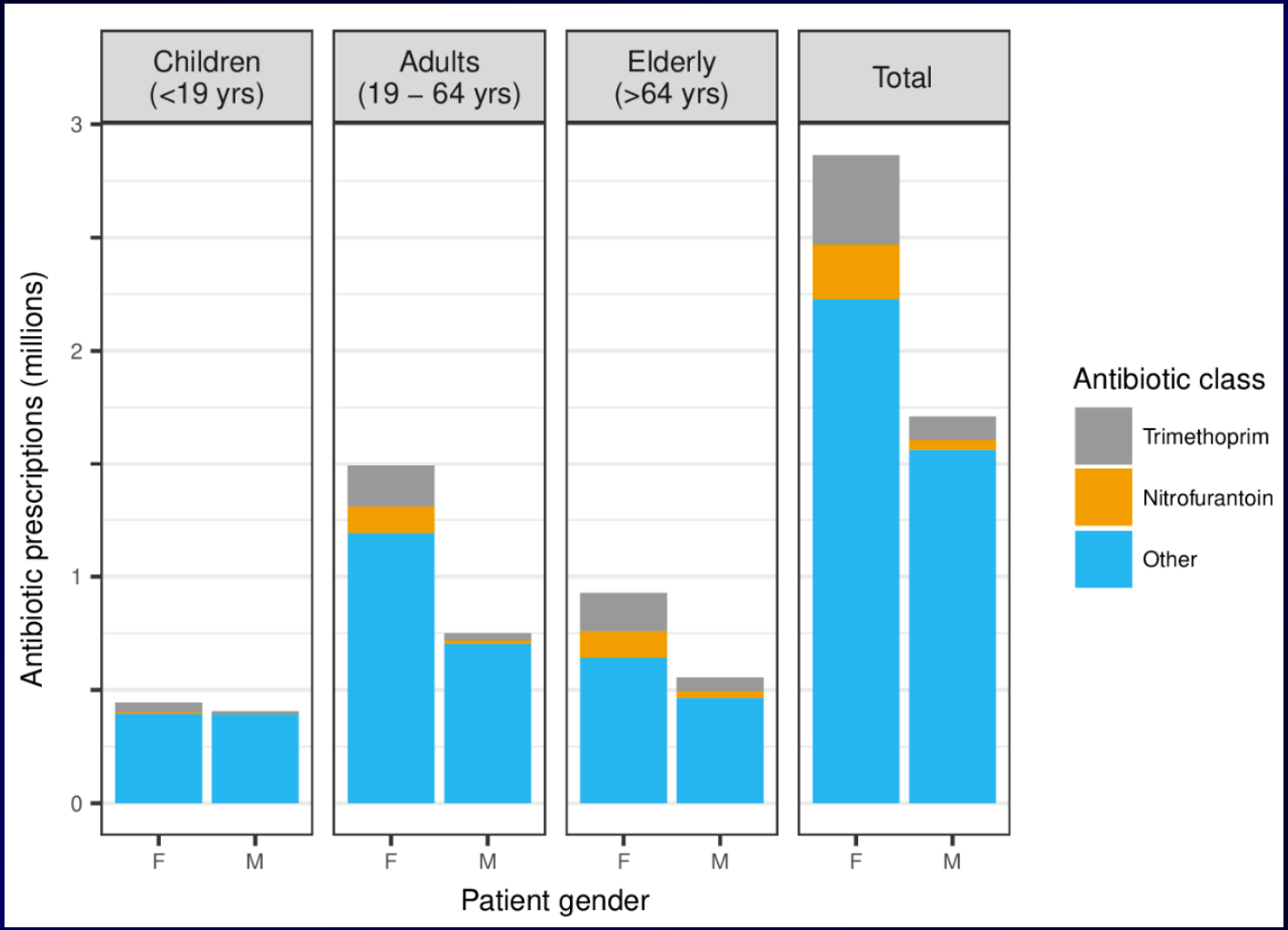
Eggermont et al. BMC Family Practice

Understanding the gender gap in antibiotic prescribing: a cross-sectional analysis of English primary care

- **STRENGHTS AND LIMITATIONS OF THIS STUDY**
- **This study is one of the first to explore the underlying causes of the large gap in the number of antibiotics prescribed to men and women in primary care.**
- **Findings are derived from a large, representative sample of primary care patients in England.**
- **Extensive mapping of diagnostic codes to clinical conditions made it possible to analyse prescribing across a range of conditions and to account for comorbidity.**
- **Identification of antibiotics that are used to treat urinary tract infection (UTI) but rarely other conditions in this setting (trimethoprim and nitrofurantoin) allowed for approximation of UTI prescribing despite incomplete diagnostic coding.**
- **The data do not include indicators of antibiotic appropriateness, such as severity of illness, and so the clinical appropriateness of gender differences in prescribing could not be evaluated.**

Smith et al. BMJ Open 2018

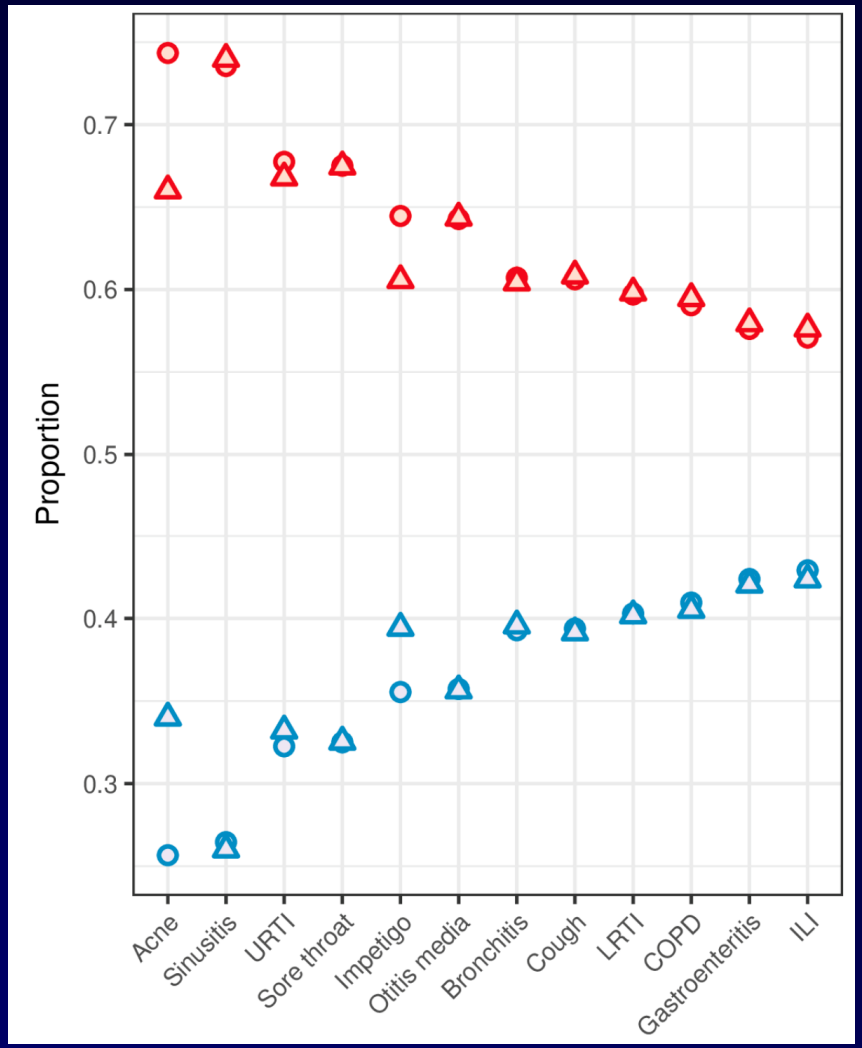
All systemic antibiotic prescriptions recorded in The Health Improvement Network (THIN) between 2013 and 2015, stratified by gender and age group



Antibiotics used to treat urinary tract infection (UTI) (trimethoprim and nitrofurantoin) are identified separately from all other antibiotics.

Smith et al. BMJ Open 2018

For common conditions in general practice, the proportions of all consultations (circles) and antibiotic prescriptions (triangles) attributed to women (red) and men (blue)



Consultations and prescriptions include all adult patients (aged 19–64) without comorbidity consulting at their primary registered practice.

Conditions are ordered by consultation proportion.

COPD, chronic obstructive pulmonary disease; ILI, influenza-like illness; LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection.

Smith et al. BMJ Open 2018

Understanding the gender gap in antibiotic prescribing: a cross-sectional analysis of English primary care

- **Conclusions** The gender gap in antibiotic prescribing can largely be explained by consultation behaviour. Although in most cases adult men and women are equally likely to be prescribed an antibiotic when consulting primary care, it is unclear whether or not they are equally indicated for antibiotic therapy.

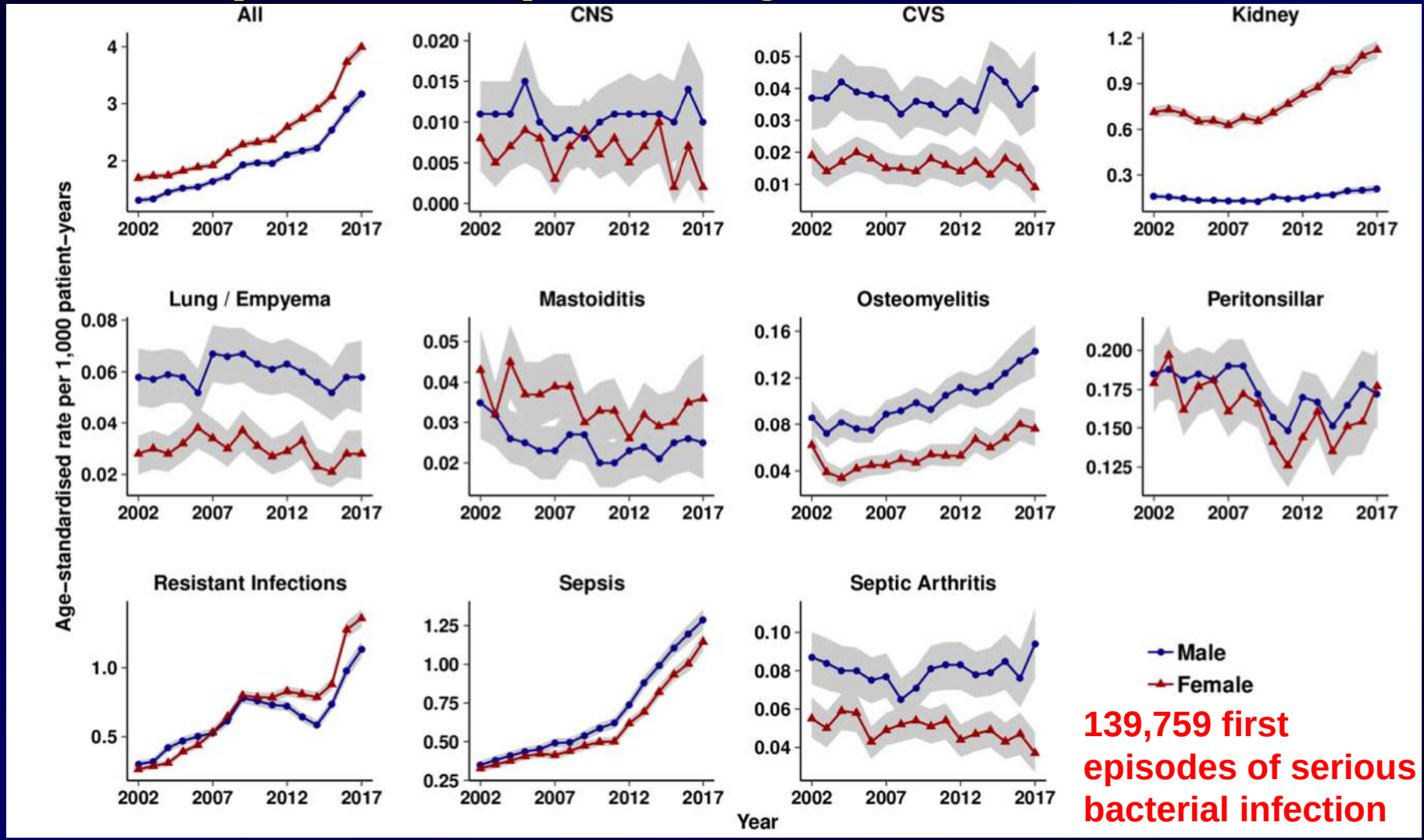
Smith et al. BMJ Open 2018

Serious bacterial infections and antibiotic prescribing in primary care: cohort study using electronic health records in the UK

- This cohort study included 10.1 million patients with 69.3 million patient-years of follow-up at 706 UK family practices from 2002 to 2017.
- The study included all antibiotic prescriptions and classified them according to the medical conditions recorded on the same date.
- Total antibiotic prescribing rate per 1000 patients/year was: male 423; female 621
- Conclusions We did not find population-level evidence that family practices with lower total antibiotic prescribing might have more frequent occurrence of serious bacterial infections overall.

Gulliford et al., BMJ 2020

Age-standardised rates of serious bacterial infections per 1000 patient-years from 2002 to 2017



Red lines, female; blue lines, male; shaded areas, 95% CIs. CNS, central nervous system; CVS, cardiovascular system.

Gulliford et al., BMJ 2020

Adjusted odds ratio for independent risk factors for multidrug resistant gram-negative bacteremia based on multivariate logistic regression analysis[a] (n=143)

Risk factors	Adjusted multivariate	
	p-value	*OR (95% CI)*
Male sex	0.02	2.98 (1.18–7.47)
Age ≥ 60 years old	0.03	2.52 (1.07–5.93)
Previous therapeutic antimicrobial use	0.04	2.45 (1.06–5.65)
Liver disease	0.02	4.91 (1.25–19.29)
Bacteremia by *Klebsiella pneumoniae*	<0.001	4.59 (1.93–70.93)

([a]) Multivariate analysis using a logistic regression model included the following variables: male sex, age ≥ 60 years old, previous therapeutic antimicrobial use, liver disease, catheter use, hospitalization in prior 6 months and bacteremia by *K. pneumoniae*

Leal et al. BMC Infectious Diseases, 20

Bloodstream infections caused by *Escherichia coli* in onco-haematological patients: Risk factors and mortality in an Italian prospective survey (n=342)

Cox regression analysis for mortality in patients with hematological malignancies and BSI caused by *Escherichia coli*

Variables	HR	(95% IC)	P values
Acute hepatic failure	9.90	(3.08–31.73)	<0.001
Septic shock	8.56	(3.33–21.95)	<0.001
Male sex	6.46	(2.19–19.01)	0.001
Refractory/Relapsed HM	3.25	(1.35–7.83)	0.008
3rd generation cephalosporins resistance by EC isolate	3.18	(1.36–7.43)	0.007

https://doi.org/10.1371/journal.pone.0224465.t004

BSI, bllodstream infections
HM, hematological malignancies

Trecarichi et al. Plos One, 2019

Andamento antibiotico-resistenza in 6887 episodi di batteriemia (3904 maschi e 2983 femmine) Regione Toscana 2019 (ARS)

	2019						
	MASCHI			*FEMMINE*			*p-value*
	N	*%*	*IC*	*N*	*%*	*IC*	
3rd generation ceph-R *Klebsiella*	731	62,0	[58,4-65,5]	442	52,3	[47,6-56,9]	0,001
Carbapenem-R *Klebsiella*	731	32,0	[28,6-35,4]	442	27,1	[23,0-31,3]	0,079
3rd generation ceph-R *E.coli*	1283	31,1	[28,6-33,6]	1220	25,8	[23,4-28,3]	0,003
FQ R *E.coli*	1283	43,8	[41,1,-46,5]	1220	41,1	[33,7-39,1]	<0,001
Carbapenem-R *Pseudomonas*	325	9,8	[6,7-13,1]	186	9,1	[5,0-13,3]	0,794
Carbapenem-R *Acinetobacter*	95	66,3	[56,7-75,9]	75	54,7	[43,3-66,0]	0,122
MRSA	797	26,1	[23,0-29,2]	515	23,3	[19,6-27,0]	0,253
Vanco-R *Enterococcus faecium*	226	19,0	[13,9-24,2]	163	12,3	[7,2-17,3]	0,074

K. Pneumoniae, resistenza cefalosporine III generazione per classe di età e sesso ARS Toscana 2019

K. Pneumoniae, resistenza carbapenemi per classe di età e sesso ARS Toscana 2019

E. coli, resistenza cefalosporine III generazione per classe di età e sesso ARS Toscana 2019

E. coli, resistenza fluorochinoloni per classe di età e sesso ARS Toscana 2019

Acinetobacter spp., resistenza carbapenemi per classe di età e sesso ARS Toscana 2019

Conclusioni

- La prescrizione di antibiotici prevale nel sesso femminile in molti paesi (maggior numero di visite delle donne nell'ambulatorio del medico di famiglia)
- I dati sull'antibiotico-resistenza di genere sono carenti nella letteratura internazionale
- Le poche pubblicazioni ne riportano una prevalenza nel sesso maschile